

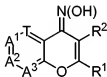
Applicants: Jeremy Green et al.
Application No.: 10/808,678

THE CLAIMS

Following is a listing of claims:

1-46. (Canceled)

47. (Previously presented) A composition comprising an effective amount of a compound of formula I:



I

or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, adjuvant, or vehicle, wherein:

R¹ is -(L)_mR, -(L)_mAr¹, or -(L)_mCy¹;

L is -S-, -O-, -N(R)-, or a C₁₋₆ alkylidene chain wherein up to two non-adjacent methylene units of L are optionally and independently replaced by -S-, -O-, -N(R)-, -N(R)C(O)-, -N(R)C(S)-, -N(R)C(O)N(R)-, -N(R)C(S)N(R)-, -N(R)CO₂-, -C(O)-, -CO₂-, -C(O)N(R)-, -C(S)N(R)-, -OC(O)N(R)-, -SO₂-, -SO₂N(R)-, -N(R)SO₂-, -N(R)SO₂N(R)-, -C(R)=NN(R)-, -C(R)=N-O(R)-, -C(O)C(O)-, or -C(O)CH₂C(O)-;

m is 0 or 1;

Ar¹ is an optionally substituted 5-7 membered monocyclic ring or an 8-10 membered bicyclic ring having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

Cy¹ is an optionally substituted 3-7 membered saturated or partially unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-10 membered saturated or partially unsaturated bicyclic

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ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein;

Ar¹ and Cy¹ are each optionally substituted with up to 5 occurrences of Z-R^X; wherein each occurrence of Z is independently a bond or a C₁₋₆ alkylidene chain, wherein up to two non-adjacent methylene units of Z are optionally replaced by -S-, -O-, -N(R)-, -N(R)C(O)-, -N(R)C(S)-, -N(R)C(O)N(R)-, -N(R)C(S)N(R)-, -N(R)CO₂-, -C(O)-, -CO₂-, -C(O)N(R)-, -C(S)N(R)-, -OC(O)N(R)-, -SO₂-, -SO₂N(R)-, -N(R)SO₂-, -N(R)SO₂N(R)-, -C(R)=NN(R)-, -C(R)=N-O(R)-, -C(O)C(O)-, or -C(O)CH₂C(O)-;

each occurrence of R^X is independently selected from -R', halogen, NO₂, CN, -OR', -SR', -N(R')₂, -N(R')C(O)R', -N(R')C(S)R', -N(R')C(O)N(R')₂, -N(R')C(S)N(R')₂, -N(R')CO₂R', -C(O)R', -C(S)R', -CO₂R', -OC(O)R', -C(O)N(R')₂, -C(S)N(R')₂, -OC(O)N(R')₂, -S(O)R', -SO₂R', -S(O)₃R'; -SO₂N(R')₂, -N(R')SO₂R', -N(R')SO₂N(R')₂, -C(O)C(O)R', -C(O)CH₂C(O)R', -NR'NR'C(O)R', -NR'NR'C(O)N(R')₂, -NR'NR'CO₂R', -C(O)N(OR')R', -C(NOR')R', -S(O)₃R', -N(OR')R', -C(=NH)-N(R')₂; or -(CH₂)₀₋₂NHC(O)R'; wherein

each occurrence of R is independently hydrogen or an optionally substituted C₁₋₆ aliphatic group,

each occurrence of R' is independently hydrogen or an optionally substituted C₁₋₆ aliphatic group, an optionally substituted C₆₋₁₀ aryl ring, an optionally substituted heteroaryl ring having 5-10 ring atoms, or an optionally substituted heterocyclyl ring having 3-10 ring atoms; or

R and R' or two occurrences of either R or R' are taken together with the atoms to which they are bound to form an optionally substituted 5-8 membered saturated, partially unsaturated, or aryl ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or

two occurrences of either R' or R on the same nitrogen are taken together with the nitrogen atom to which they are bound to form an optionally substituted 5-8

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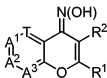
membered saturated, partially unsaturated, or aryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;
 R^2 is hydrogen, CN, -SR, -OR, -CO₂R, -OC(O)R, -C(O)R, -C(O)N(R)₂, -N(R)₂, or -N(R)C(O)R;
T is CR³;
each of A¹, A², and A³ is, independently, CR⁴;
 R^3 is selected from hydrogen, halogen, NO₂, CN, -SR, -OR, -N(R)₂, or an optionally substituted C₁₋₆ aliphatic group; and
 R^4 is selected from halogen, NO₂, CN, -(L)_mR, -(L)_mAr¹, or -(L)_mCy¹; or
two R⁴ groups on adjacent atoms are taken together to form an optionally substituted 5-7 membered partially unsaturated or fully unsaturated ring having 0-3 heteroatoms independently selected from oxygen, sulfur, or nitrogen, wherein;
each ring formed by two R⁴ groups on adjacent atoms taken together is optionally substituted with up to 4 occurrences of Z-R^x.

48. (Canceled)

49. (Previously presented) The composition of claim 47, additionally comprising a therapeutic agent selected from mechlorethamine, chlorambucil, cyclophosphamide, melphalan, ifosfamide, methotrexate, 6-mercaptopurine, 5-fluorouracil, cytarabine, gemcitabine, vinblastine, vincristine, vinorelbine, paclitaxel, etoposide, irinotecan, topotecan, doxorubicin, bleomycin, mitomycin, carmustine, lomustine, cisplatin, carboplatin, asparaginase, and tamoxifen, leuprolide, flutamide, megestrol, imatinib (GleevecTM), adriamycin, dexamethasone, or cyclophosphamide.

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50. (Previously presented) A method of inhibiting c-MET kinase activity in a biological sample, wherein said biological sample is selected from a cell culture, biopsied material obtained from a mammal, saliva, urine, feces, semen, or tears, or an extract thereof; which method comprises contacting said biological sample with a composition according to claim 47 or a compound of formula I:



or a pharmaceutically acceptable salt thereof, wherein:

R¹ is -(L)_mR, -(L)_mAr¹, or -(L)_mCy¹;

L is -S-, -O-, -N(R)-, or a C₁₋₆ alkylidene chain wherein up to two non-adjacent methylene units of L are optionally and independently replaced by -S-, -O-, -N(R)-, -N(R)C(O)-, -N(R)C(S)-, -N(R)C(O)N(R)-, -N(R)C(S)N(R)-, -N(R)CO₂-, -C(O)-, -CO₂-, -C(O)N(R)-, -C(S)N(R)-, -OC(O)N(R)-, -SO₂-, -SO₂N(R)-, -N(R)SO₂-, -N(R)SO₂N(R)-, -C(R)=NN(R)-, -C(R)=N-O(R)-, -C(O)C(O)-, or -C(O)CH₂C(O)-; m is 0 or 1;

Ar¹ is an optionally substituted 5-7 membered monocyclic ring or an 8-10 membered bicyclic ring having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

Cy¹ is an optionally substituted 3-7 membered saturated or partially unsaturated monocyclic ring having 0-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur, or an 8-10 membered saturated or partially unsaturated bicyclic ring system having 0-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur, wherein;

Ar¹ and Cy¹ are each optionally substituted with up to 5 occurrences of Z-R^X; wherein

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each occurrence of Z is independently a bond or a C₁₋₆ alkylidene chain, wherein up to two non-adjacent methylene units of Z are optionally replaced by -S-, -O-, -N(R)-, -N(R)C(O)-, -N(R)C(S)-, -N(R)C(O)N(R)-, -N(R)C(S)N(R)-, -N(R)CO₂-, -C(O)-, -CO₂-, -C(O)N(R)-, -C(S)N(R)-, -OC(O)N(R)-, -SO₂-, -SO₂N(R)-, -N(R)SO₂-, -N(R)SO₂N(R)-, -C(R)=NN(R)-, -C(R)=N-O(R)-, -C(O)C(O)-, or -C(O)CH₂C(O)-;

each occurrence of R^X is independently selected from -R', halogen, NO₂, CN, -OR', -SR', -N(R')₂, -N(R')C(O)R', -N(R')C(S)R', -N(R')C(O)N(R')₂, -N(R')C(S)N(R')₂, -N(R')CO₂R', -C(O)R', -C(S)R', -CO₂R', -OC(O)R', -C(O)N(R')₂, -C(S)N(R')₂, -OC(O)N(R')₂, -S(O)R', -SO₂R', -S(O)₃R'; -SO₂N(R')₂, -N(R')SO₂R', -N(R')SO₂N(R')₂, -C(O)C(O)R', -C(O)CH₂C(O)R', -NR'NR'C(O)R', -NR'NR'C(O)N(R')₂, -NR'NR'CO₂R', -C(O)N(OR')R', -C(NOR')R', -S(O)₃R, -N(OR')R', -C(=NH)-N(R')₂; or -(CH₂)₀₋₂NHC(O)R'; wherein

each occurrence of R is independently hydrogen or an optionally substituted C₁₋₆ aliphatic group,

each occurrence of R' is independently hydrogen or an optionally substituted C₁₋₆ aliphatic group, an optionally substituted C₆₋₁₀ aryl ring, an optionally substituted heteroaryl ring having 5-10 ring atoms, or an optionally substituted heterocyclyl ring having 3-10 ring atoms; or

R and R' or two occurrences of either R or R' are taken together with the atoms to which they are bound to form an optionally substituted 5-8 membered saturated, partially unsaturated, or aryl ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur; or

two occurrences of either R' or R on the same nitrogen are taken together with the nitrogen atom to which they are bound to form an optionally substituted 5-8 membered saturated, partially unsaturated, or aryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

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R^2 is hydrogen, CN, -SR, -OR, -CO₂R, -OC(O)R, -C(O)R, -C(O)N(R)₂, -N(R)₂,
-N(R)C(O)R, or an optionally substituted C₁₋₆ aliphatic group;

T is CR³;

each of A¹, A², and A³ is, independently, CR⁴;

R³ is selected from hydrogen, halogen, NO₂, CN, -SR, -OR, -N(R)₂, or an optionally
substituted C₁₋₆ aliphatic group; and

R⁴ is selected from halogen, NO₂, CN, -(L)_mR, -(L)_mAr¹, or -(L)_mCy¹; or

two R⁴ groups on adjacent atoms are taken together to form an optionally
substituted 5-7 membered partially unsaturated or fully unsaturated ring
having 0-3 heteroatoms independently selected from oxygen, sulfur, or
nitrogen, wherein;

each ring formed by two R⁴ groups on adjacent atoms taken together is optionally
substituted with up to 4 occurrences of Z-R^X.

51. (Canceled)

52. (Previously presented) A method of treating or lessening the severity of a disease
or condition in a patient selected from gastric cancer, pancreatic cancer, ovarian cancer,
breast cancer, or prostate cancer comprising the step of administering to said patient a
composition of claim 47.

53. (Previously presented) The method according to claim 52, comprising the
additional step of administering to said patient an additional therapeutic agent selected
from mechlorethamine, chlorambucil, cyclophosphamide, melphalan, ifosfamide,
methotrexate, 6-mercaptopurine, 5-fluorouracil, cytarabine, gemcitabine, vinblastine,
vincristine, vinorelbine, paclitaxel, etoposide, irinotecan, topotecan, doxorubicin,
bleomycin, mitomycin, carmustine, lomustine, cisplatin, carboplatin, asparaginase, and

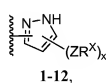
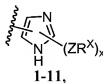
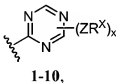
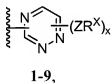
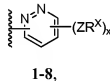
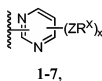
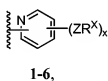
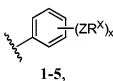
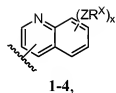
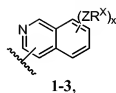
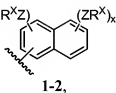
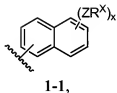
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tamoxifen, leuprolide, flutamide, megestrol, imatinib (Gleevec™), adriamycin, dexamethasone, or cyclophosphamide, wherein:

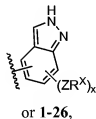
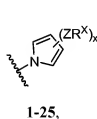
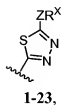
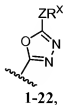
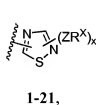
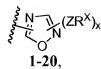
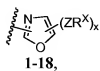
said additional therapeutic agent is appropriate for the disease being treated; and
said additional therapeutic agent is administered together with said composition
as a single dosage form or separately from said composition as part of a
multiple dosage form.

54-58. (Canceled)

59. (Previously presented) The composition according to claim 47, wherein R^1 is $-(L)_mAr^1$ and Ar^1 is selected from one of the following groups:

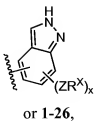
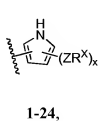
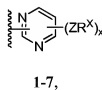
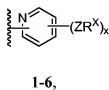
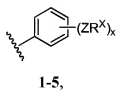


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wherein x is 0-5.

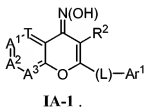
60. (Previously presented) The composition according to claim 59, wherein Ar¹ is selected from one of the following groups:



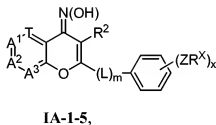
wherein x is 0-5.

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61. (Previously presented) The composition according to claim 59, wherein R^1 is $-(L)_m-Ar^1$, m is 1 and compounds have the formula **IA-1**:

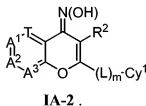


62. (Previously presented) The composition according to claim 59, wherein Ar^1 is phenyl with 0-5 occurrences of ZR^x and compounds have the formula **IA-1-5**:



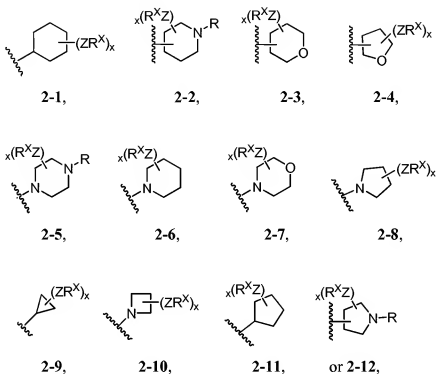
wherein x is 0-5.

63. (Previously presented) The composition according to claim 47, wherein R^1 is $-(L)_m-Cy^1$ and compounds have the formula **IA-2**:



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64. (Previously presented) The composition according to claim 63, wherein Cy^1 is selected from one of the following groups:



wherein x is 0-5.

65. (Previously presented) The composition according to claim 59, wherein L is an optionally substituted C_{1-6} straight or branched alkylidene chain wherein one methylene unit of L is optionally replaced by O, NR, NRCO, NRCS, NRCONR, NRCSNR, NR CO_2 , CO, CO_2 , CONR, CSNR, OC(O)NR, SO_2 , SO_2NR , NR SO_2 , NR SO_2NR , C(O)C(O), or C(O)CH $_2$ C(O).

66. (Previously presented) The composition according to claim 65, wherein L is an optionally substituted C_{1-6} straight or branched alkylidene chain wherein one methylene unit of L is optionally replaced by O, NR, NRCO, CO, CONR, SO_2NR , NR SO_2 .

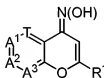
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67. (Previously presented) The composition according to claim 47, wherein R^1 is $-(L)_mR$, L is an optionally substituted C_{1-6} straight or branched alkylidene chain wherein one methylene unit of L is optionally replaced by O, NR, NRCO, NRCONR, NR CO_2 , CO, CO_2 , CONR, OC(O)NR, SO_2 , SO_2NR , $NRSO_2$, $NRSO_2NR$, and R is an optionally substituted C_{1-6} aliphatic group.

68. (Previously presented) The composition according to claim 47, wherein R^2 is hydrogen, -CN, -OR, $-CO_2R$, $-OC(O)R$, $-C(O)R$, $-C(O)N(R)_2$, $-N(R)_2$, or $-N(R)C(O)R$.

69-70. (Canceled)

71. (Previously presented) The composition according to claim 47, wherein R^2 is hydrogen and compounds have the formula **IB**:



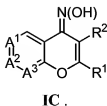
IB .

72. (Previously presented) The composition according to claim 47, wherein T is CR^3 and R^3 is hydrogen, halogen, CN, or an optionally substituted C_{1-6} aliphatic group.

73. (Previously presented) The composition according to claim 72, wherein R^3 is hydrogen, halogen, CF_3 , methyl, ethyl, n-propyl, isopropyl, or cyclopropyl.

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74. (Previously presented) The composition according to claim 47, wherein T is CR³, R³ is hydrogen and compounds have the formula **IC**:

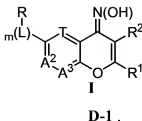


75. (Previously presented) The composition according to claim 47, wherein A¹ is CR⁴ and R⁴ is halogen, CN, -(L)_mR, -(L)_mAr¹, or -(L)_mCy¹.

76. (Previously presented) The composition according to claim 75, wherein L is an optionally substituted C₁₋₆ straight or branched alkylidene chain wherein one methylene unit of L is optionally replaced by O, NR, NRCO, NRCONR, NRCO₂, CO, CO₂, CONR, OC(O)NR, SO₂, SO₂NR, NRSO₂, NRSO₂NR, C(O)C(O), or C(O)CH₂C(O).

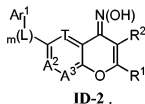
77. (Previously presented) The composition according to claim 75, wherein A¹ is CR⁴ and R⁴ is halogen, CN, or R.

78. (Previously presented) The composition according to claim 75, wherein A¹ is CR⁴, R⁴ is -(L)_mR, and compounds have the formula **ID-1**:

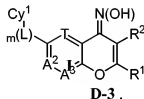


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79. (Previously presented) The composition according to claim 75, wherein A^1 is CR^4 , R^4 is $-(L)_mAr^1$, and compounds have the formula **ID-2**:



80. (Previously presented) The composition according to claim 75, wherein A^1 is CR^4 , R^4 is $-(L)_mCy^1$, and compounds have the formula **ID-3**:



81. (Previously presented) The composition according to claim 47, wherein A^2 is CR^4 and R^4 is halogen, CN, $-(L)_mR$, $-(L)_mAr^1$, or $-(L)_mCy^1$.

82. (Previously presented) The composition according to claim 81, wherein L is an optionally substituted C_{1-6} straight or branched alkylidene chain wherein one methylene unit of L is optionally replaced by O, NR, NRCO, NRCONR, NR CO_2 , CO, CO_2 , CONR, OC(O)NR, SO_2 , SO_2NR , $NRSO_2$, $NRSO_2NR$, C(O)C(O), or C(O)CH $_2$ C(O).

83. (Previously presented) The composition according to claim 81, wherein A^2 is CR^4 and R^4 is halogen or R.

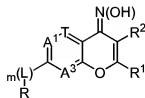
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84. (Previously presented) The composition according to claim 81, wherein A^2 is CR^4 and R^4 is $-(L)_mR$, wherein L is $-O-$ or $-N(R)-$.

85. (Previously presented) The composition according to claim 81, wherein A^2 is CR^4 , R^4 is $-(L)_mCy^1$, m is 0 and Cy^1 is **2-2**, **2-5**, **2-6**, **2-7**, **2-8**, or **2-12**.

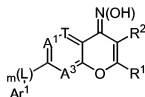
86. (Previously presented) The composition according to claim 81, wherein A^2 is CR^4 , R^4 is $-(L)_mAr^1$, m is 0 and Ar^1 is **1-5**, **1-6**, **1-11**, **1-12**, **1-13**, **1-19**, **1-24**, or **1-25**.

87. (Previously presented) The composition according to claim 81, wherein A^2 is CR^4 , R^4 is $-(L)_mR$, and compounds have the formula **IE-1**:



IE-1 .

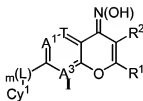
88. (Previously presented) The composition according to claim 81, wherein A^2 is CR^4 , R^4 is $-(L)_mAr^1$, and compounds have the formula **IE-2**:



IE-2 .

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89. (Previously presented) The composition according to claim 81, wherein A^2 is CR^4 , R^4 is $-(L)_mCy^1$, and compounds have the formula **IE-3**:



E-3 .

90. (Previously presented) The composition according to claim 47, wherein A^3 is CR^4 and R^4 is halogen, CN, $-(L)_mR$, $-(L)_mAr^1$, or $-(L)_mCy^1$.

91. (Previously presented) The composition according to claim 90, wherein L is an optionally substituted C₁₋₆ straight or branched alkylidene chain wherein one methylene unit of L is optionally replaced by O, NR, NRCO, NRCONR, NRCO₂, CO, CO₂, CONR, OC(O)NR, SO₂, SO₂NR, NRSO₂, NRSO₂NR, C(O)C(O), or C(O)CH₂C(O).

92. (Previously presented) The composition according to claim 90, wherein A^3 is CR^4 and R^4 is halogen or R.

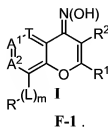
93. (Previously presented) The composition according to claim 90, wherein A^3 is CR^4 and R^4 is $-(L)_mR$, wherein L is -O- or -N(R)-.

94. (Previously presented) The composition according to claim 90, A^3 is CR^4 , R^4 is $-(L)_mCy^1$, m is 0 and Cy¹ is **2-2, 2-5, 2-6, 2-7, 2-8, or 2-12**.

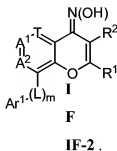
95. (Previously presented) The composition according to claim 90, wherein A^3 is CR^4 , R^4 is $-(L)_mAr^1$, m is 0 and Ar¹ is **1-5, 1-6, 1-11, 1-12, 1-13, 1-19, 1-24, or 1-25**.

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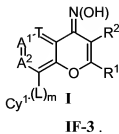
96. (Previously presented) The composition according to claim 90, wherein A^3 is CR^4 , R^4 is $-(L)_mR$, and compounds have the formula **IF-1**:



97. (Previously presented) The composition according to claim 90, wherein A^3 is CR^4 , R^4 is $-(L)_mAr^1$, and compounds have the formula **IF-2**:

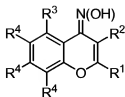


98. (Previously presented) The composition according to claim 90, wherein A^3 is CR^4 , R^4 is $-(L)_mCy^1$, and compounds have the formula **IF-3**:



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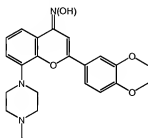
99. (Previously presented) The composition according to claim 47, wherein T is CR³, A¹, A² and A³ are each CR⁴ and compounds have the formula **IG-1**:



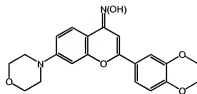
IG-1.

100. (Previously presented) The composition according to claim 47, wherein each ZR^x is independently halogen, NO₂, CN, or an optionally substituted group selected from C₁₋₄ alkyl, aryl, aralkyl, -N(R')₂, -CH₂N(R')₂, -OR', -CH₂OR', -SR', -CH₂SR', -COOR', or -S(O)₂N(R')₂.

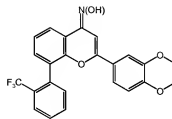
101. (Previously presented) The composition according to claim 47, selected from one of the following compounds:



I-1,

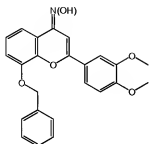


I-2,

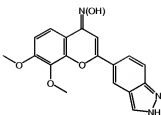


I-3,

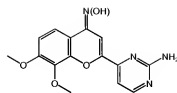
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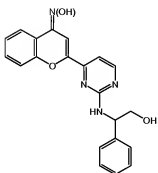
I-4,



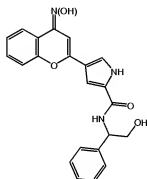
I-5,



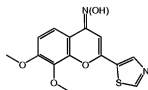
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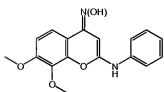
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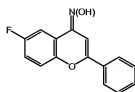
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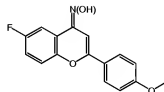
I-9,



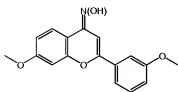
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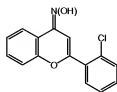
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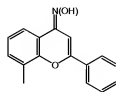
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I-13,

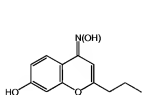


I-14,

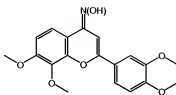


I-15,

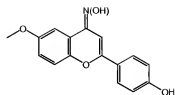
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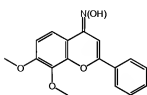
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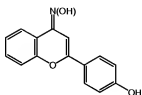
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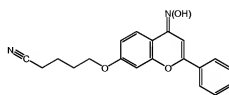
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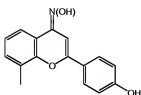
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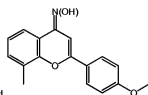
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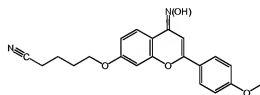
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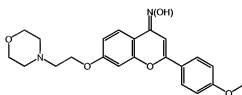
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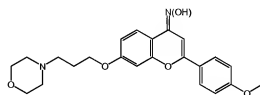
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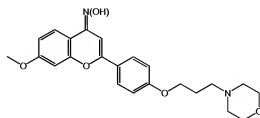
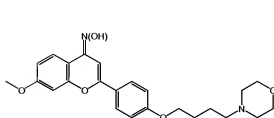
I-24,



I-25,

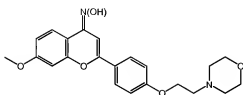


I-26,

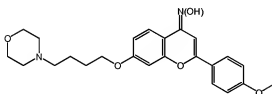


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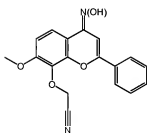
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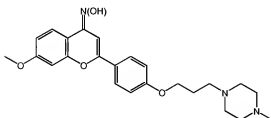
I-29,



I-31,

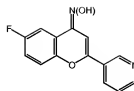


I-33,

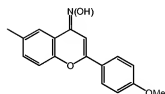


I-35,

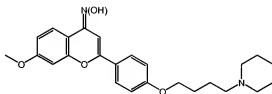
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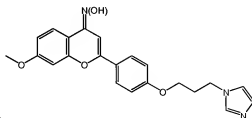
I-30,



I-32,

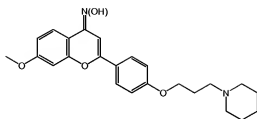


I-34,



I-36,

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or I-37 .